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EXPERIENCES WITH THE USE OF RESERPINE ON THE CHRONICALLY DISTURBED MENTAL PATIENT

H. A. Luiz, M.B., B.Ch.

Komani Hospital, Queenstown

Since the use of Reserpine was introduced in psychiatric institutions varied reports have been published on the efficacy of the drug in the chronically-disturbed mental patient. The lay press has hailed it as a panacea for diverse mental ailments with such effect that we have been approached by relatives of patients requesting its use. Unfortunately our initial experiences were not in accordance with the claims made by other observers. We used initial supplies with caution. The dosage seldom exceeded 3 mg. per diem and the duration of treatment was usually 1 month. The response obtained was unsatisfactory and further trials were discontinued.

On further discussion with the manufacturer's representative we came to the conclusion that the discrepancy between our results and those published in the journals were possibly due to (*a*) insufficient doses or (*b*) premature discontinuation of therapy. It was therefore decided to recommence trials with larger doses used over a longer period.

TRIAL SERIES

For this series 17 of the most disturbed patients in the refractory ward were selected. Of these, 12 were chronic schizophrenics and 5 suffered from epileptic psychosis. Trials were begun on moderate doses of 1 mg. orally or intramuscularly per diem, gradually increased until the appearance of untoward side-effects led us to consider further increases an unjustifiable risk.

All but 2 of the patients were disordered to the extent that most of our observations were entirely objective. The main guides to the effect of the drug and dosage control were the response of the cardiovascular system and changes in the general behaviour of the patient.

Non-Epileptic Cases

To deal first with the patients who were not suffering from epilepsy, it was noted that in 3 cases oral doses would be increased up to 10 mg. daily while in the others the doses varied from 4 to 8 mg. daily. The shortest period required to reach the optimum dose was 3 weeks, and the longest 8 weeks. Too rapid an increase in dosage often resulted in hypotension and bradycardia. This was overcome by reducing the dose for another 7 days before increasing to a desired maximum. Resort was had to intramuscular and intravenous use only in cases of extreme negativism when the patient could not be coaxed into taking oral medication. With these parenteral routes of administration untoward side-effects appeared much earlier and in a more marked degree. During the 2nd week of the trials patients could be encouraged to take the tablets orally. Tact and patience are essential on the part of the nursing staff to steer them through this phase. With intramuscular medication it was found unnecessary to use more than 3 mg. a day or to continue it for longer than 10 days. No fixed dosage-schedule can be presented, for it was found that individual responses varied.

Attempts to work out a schedule according to the patient's weight and pre-trial blood-pressure readings produce inconsistent results.

Before the trials these patients were the most difficult nursing problems in the ward. They were unapproachable, destructive and violent, requiring heavy sedation and maintenance electroplexy regularly. Their condition can briefly be described as chronically excited mental disorganization with explosive episodes, some in response to apparently fixed delusions and others apparently motiveless. One patient suffering from chronic schizophrenia of over 20 years' standing, unresponsive to all the routine forms of electrical and drug restraint commonly used, required on an average 5 hours' seclusion daily.

Of the 12 schizophrenics, trials were discontinued in 4 because of the persistence of undesirable reactions or untoward physiological effect. In the remaining 8 patients it was noticed that there was a gradual but generalized decline of psychomotor activity. Explosive

episodes became less frequent and eventually ceased. The patients were more subdued, and capable of carrying out simple instructions, and they managed to adjust themselves more satisfactorily to the ward routine. It was disappointing to note that at no time was the basic pattern of the psychosis altered in any respect. The 3 phases noted by Barsa & Kline[1] were not conspicuous and we tended to regard them as the exception rather than the rule. The shortest period that elapsed before noticeable response was obtained was 5 weeks, and the longest 16 weeks. Physically, each patient put on an average of 9 lb. in weight. There were no dietery alteration introduced during the trials and we concluded that the increase in weight was the direct result of the insidiously progressive inertia on the same calorie intake as obtained before the trials. It was pleasing to note that although the patients were more at ease with their environment the narcotizing effect so commonly found with the use of the opiates, barbiturates and paraldehyde were completely absent. Rapport could be established with the patients at any time and they could be roused from sleep without any signs of undue drowsiness. We found that eventually we could eliminate all other sedation. During the early stages of the trials we were compelled to prescribe decreasing doses of the sedatives which were being used on the patients before the trials. The most satisfactory and safest of these was paraldehyde, the effects of which appeared to be enhanced on our Reserpine patients.

Epileptic Psychosis

Patients suffering from epileptic psychosis, especially those of long standing and deteriorated types, are generally speaking a nursing problem in mental hospitals. Most require heavy doses of phenobarbitone used in conjunction with one or other of the anti-convulsants to suppress their seizure rate. They eventually become drowsy and retarded, living a mechanical sort of existence, and with time exhibit the neurotoxic effects of continuous phenobarbitone medication. On the rationale that if the sedative effect of Reserpine could replace that of phenobarbitone, there might be a change for the better. Twelve male non-Europeans were selected for this trial and the phenobarbitone was gradually replaced by the Reserpine over a period of a week. There was a dramatic increase in the frequency of major seizures and trials were discontinued after 14 days. In the 5 epileptic patients selected in our series of 17 in the refractory ward, it was thus decided to use Reserpine in conjunction with the phenobarbitone-anticonvulsant routine. It was found within a fortnight that there was a slight increase in the rate of seizures and no beneficial effect on the general behaviour. Furthermore the side-effects of the drug appeared to be more prominent. According to the *Lancet*[2] Reserpine facilitates convulsions in epileptics and antagonizes the effect of phenytoin. It suggests that the 2 drugs should not be used together.

Side-Effects

These usually presented themselves during the induction period. Frequently they were the result of too rapid an increase in dosage and could be controlled by moderation of the dosage. Once the patients had been stabilized we did not notice any unusual reactions. A satisfactory aspect of the side-effects was that they were all reversable on withdrawal of the drug. The following were the most troublesome that we noticed during our trials:

(*a*) *Hypotension and Bradycardia.* These are listed together because there appeared to be a proportionate relationship in their variations. It is claimed that Reserpine has little or no effect on the normotensive patient. Our experience was that there was a drop of up to 10 mm. Hg. in both systolic and diastolic readings. The degree of bradycardia, accompanied by an appreciable fall in pulse volume, was alarming at times. The slowest pulse-rate witnessed was 38 per minute. This responded to nikethamide within 2 hours, and to a subsequent reduction in dosage of Reserpine. It was noted that the blood pressure and pulse-rate were influenced by exercise. In patients examined immediately after a phase of excitement the readings returned to normal. At rest they were found to be below normal (normal being taken as the pre-trial readings of the individual patient). Once the patient had been stabilized we did not notice any undue signs in this respect.

(*b*) *Decrease in Exercise Tolerance.* Because of the uncooperative disposition of the patients no precise tests of exercise tolerance could be performed, but in all the cases after moderate exercise the increased respiratory and pulse rates, plus the general demeanour of the patients, led us to conclude that the exercise tolerance of the individual was definitely reduced in comparison with the patient's pre-trial behaviour. This is to a certain extent desirable in a chronically excited patient but the extreme should be avoided by dosage modification.

(*c*) *Mental Depression.* As most of our observations were objective the assessment of this symptom was difficult. One of our epileptics lapsed into a state of acute depression which did not respond to the usual recommended antidotes and only to drug withdrawal.

(*d*) *Aggravation of the Psychosis* caused by fears produced by the physical effects of the drug. Two of the cases managed to convey that they experienced sensations that they were suffocating. They reacted by becoming aggressive and violent. We terminated therapy during the 3rd week.

(*e*) *Tachycardia.* A persistent tachycardia was observed in 2 cases. They both presented signs of cardiac inefficiency of such severity and persistence that we discontinued trials. The first case was suffering from a well-compensated mitral stenosis before the trials; in the second we could find no organic relationship. Both presented the signs late in the 2nd week of the trials.

Contra-indications to Reserpine

Physical contra-indications are fortunately few. In hypotensive states the drug, although not absolutely contra-indicated, should be used with caution. Further study of the effect of heavy doses of Reserpine in the presence of organic heart-disease should prove interesting.

Psychiatric contra-indications include the following:

1. *Certain depressed states.* Although not included in the series reported above, we have treated 3 cases

where it was apparent that the depression was precipitated by the injudicious use of Reserpine-like drugs: (1) A psychoneurotic anxiety reaction appearing in the involutional period of European male; (2) an elderly European male suffering from psychosis with cerebral arteriosclerosis, who was restless and agitated; (3) an elderly European female being treated for hypertension with a Reserpine-like drug. All three presented a picture of severe depression which was not relieved by withdrawal of the drug, and were subsequently compelled to undergo a course of electric shock therapy for relief. We thus concluded that the use of the drug in depressed states should be limited.

2. *Epileptic psychosis.* See above.

3. *Electric shock therapy.* We have had occasion to administer shock therapy to a patient in a state of acute mania who was on Reserpine. This was followed by a state of physical shock and the patient was resuscitated with difficulty. Further cases have been quoted in the literature.[3]

CONCLUSION

We now conclude from the results obtained in our trials that Reserpine will establish itself in institutional psychiatry. It has supplied us with another means of drug restraint and facilitated the nursing of disturbed mental patients. It has introduced a new atmosphere into the refractory ward and there is a possibility that with its more widespread use maintenance electric shock therapy may be reduced by 60%. Unfortunately, in chronic cases it has produced no recoveries nor had any influence on the hospital discharge rate.

Another factor to be considered is whether it will be necessary to continue the medication indefinitely or whether it will be possible to discontinue it after the patients have been stabilized at a satisfactory level for a determined period.

SUMMARY

Reserpine was tried in 17 cases in a psychiatric refractory ward. Of the 17 cases on trial, therapy had to be discontinued in 9 because of the persistence of unsatisfactory side-reactions. Of the 8 remaining cases all were subdued and showed a satisfactory response. No recoveries were produced but the response obtained has led us to believe that its more widespread use in chronically-excited mental patients is justifiable. In the cases which responded to the drug all other sedatives and maintenance electroplexy have been dispensed with.

I wish to thank Dr. I. Vermooten, the Commissioner for Mental Hygiene, for permission to publish the article and Dr. K. B. Wright, Physician Superintendent of Komani Hospital, Dr. R. D. Kennedy and Dr. N. v.d. Westhuizen for their encouragement and criticism of the paper.

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1. Barsa, J. A. and Kline, N. S. (1956): Amer. J. Psychiat., **112**, 684.
2. Editorial (1955): Lancet, **2**, 1326.
3. Kalinowsky, L. B. (1956): Amer. J. Psychiat., **112**, 745.

THE BENEVOLENT FUND : DIE LIEFDADIGHEIDSFONDS

The following contributions to the Benevolent Fund during August and September 1956, are gratefully acknowledged.

Votive Cards in Memory of:

Dr. H. Haden *by* The Doctors and Staff of General Hospital, Johannesburg and Staff and Students of the University Physiotherapy Department.

Mr. Percy Granger *by* Dr. W. P. Mulligan.

Col. H. Buist *by* Dr. W. P. Mulligan and Dr. G. P. de Kock.

Dr. J. Gie *by* Dr. W. P. Mulligan and Dr. H. O. Hofmeyr.

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Dr. M. Gorfinkel *by* Dr. P. Leftwich.

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Dr. R. N. Pringle *by* King Williams Town Division of Medical Association of South Africa.

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Mother of Dr. K. B. Vetten *by* Dr. J. Durham and Mr. E. B. Trehair.

Mrs. G. D. de Swardt *by* Drs. Samuels, Komins and Morris.

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Dr. David Sischy *by* Drs. J. Wolfowitz, B. L. Shaff, S. Javett and S. Hoffman.

Dr. C. W. F. MacKay *by* Drs. Maxwell Margo and G. G. Henderson.

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Dr. T. W. Mills	£1	0	0
Cape Western Branch Members (Collection Box)	3	3	6
Mrs. Mary Parker	1	0	0
Cape Western Branch Members (Collection Box)	2	8	9
Dr. R. H. Johnson	0	10	6
Dr. M. R. J. Peters	0	10	6
Total	£125	16	3

South African Medical Journal

Suid-Afrikaanse Tydskrif vir Geneeskunde

EDITORIAL

REDUCING DIETS

It has long been known that restriction of calorie intake is the most important factor in the loss of excess weight. The traditional medical advice to patients wanting to reduce always includes a 'diet sheet' which, if it is scrupulously followed, cuts down the calorie intake to below the level supposed to be necessary for the maintenance of a dietary equilibrium. Experience has shown that this measure does not always lead to weight loss. Although discrepancies are usually attributed to failure or inability of the patient to carry out his instructions, the frequency of the experience has been noted. Moreover, slight departures from—not restrictions of—the normal diet appear sometimes to lead to loss of weight, and one set of workers found in a test series that persons on a high-fat diet lost weight more rapidly than those on high-protein or high-carbohydrate diets.[1] This uncertainty led Kekwick and Pawan[2] to examine the relation of calorie intake to obesity a little more closely. The question that these workers set themselves to answer was this: Is it the restriction of total calorie intake that causes the weight loss, or is it the alteration in proportions of carbohydrate, fat and protein in the diet? The normal sedentary worker—it is usually stated—takes his daily 2,200 calories as 12% of protein, 24% of fat and 64% of carbohydrate, while the average reducing diet (yielding about 1,000 calories a day) consists of protein, fat and carbohydrate in about equal proportions. Kekwick and Pawan's experiment was conducted on cases of obesity in a hospital ward under the most favourable conditions; none of the patients could 'sneak' any food and rigid biochemical controls (water retention, nitrogen balance, fat absorption) were performed. The patients fell into 3 groups for the purpose of the experiment, viz.:

1. A group fed on a diet of which the component proportions were the same (protein 20, fat 33, carbohydrate 47) but the total amounts varied (500, 1,000 1,500 and 2,000 calories).

2. A group fed on a diet of which the total calorie-content was fixed (1,000 calories) but the components

VAN DIE REDAKSIE

VERSLANKINGSDIËTE

Dit is lank reeds bekend dat beperking van kalorie-opname die belangrikste faktor by die verlies van oortollige gewig is. Die tradisionele mediese advies aan pasiënte wat gewig wil verloor, sluit altyd 'n ‚dieet-kaart' in wat, as dit stip gevolg word, die kalorie-opname verminder tot onder die peil wat vermoedelik nodig is om 'n dieet-ewewig in stand te hou. Ondervinding het getoon dat hierdie maatreël nie altyd gewigsverlies veroorsaak nie. Alhoewel teenstrydighede gewoonlik toegeskryf word aan die pasiënt se versuim of onvermoë om sy instruksies uit te voer, is daar op gelet hoe dikwels ondervinding homself herhaal. Bowendien skyn dit of geringe afwykings—en nie beperkings nie—van die normale dieet somtyds tot gewigsverlies lei, en een groep navorsers het, deur middel van 'n toetsreeks, gevind dat persone op 'n dieet met 'n hoë vetgehalte, vinniger gewig verloor het as diegene wat op 'n dieet 'n hoë proteïen- of hoë koolhidraatgehalte, was.[1] Hierdie onsekerheid het Kekwick en Pawan[2] daartoe gelei om die betrekking wat kalorie-opname op vetsug het, ietwat nader te ondersoek. Die vraag wat hierdie navorsers aan hulself gestel het om te beantwoord, was: Is dit die beperking van algehele kalorie-opname wat die gewigsverlies veroorsaak, of is dit verandering van die verhoudings tussen koolhidraat, vet en proteïen in die dieet wat dit veroorsaak?

Die normale, sittende werker—so word gewoonlik verklaar—neem sy daaglikse 2,200 kaloriëe in die vorm van 12% proteïen, 24% vet en 64% koolhidraat op, terwyl die gemiddelde verslankingsdieet (wat sowat 1,000 kalorieë per dag lewer), uit ongeveer gelyke verhoudings van proteïen, vet en koolhidraat bestaan. Kekwick en Pawan se eksperiment is uitgevoer op gevalle van vetsug in 'n hospitaalsaal onder die gunstigste omstandighede; geeneen van die pasiënte kon enige voedsel ‚insmokkel' nie, en streng biochemiese kontrole (waterbehoud, stikstofbalans en vet-opname) is uitgevoer. Vir eksperimentele doeleindes, het hulle die pasiënte in 3 groepe ingedeel, naamlik:

1. 'n Groep gevoed op 'n dieet waarvan die samestellende verhoudings dieselfde was (proteïen 20, vet 33, koolhidraat 47), maar waarvan die totale hoeveelhede afgewissel het (500, 1,000, 1,500 en 2,000 kalorieë).

2. 'n Groep gevoed op 'n dieet waarvan die totale kalorie-inhoud vasgestel was (1,000 kalorieë), maar waarvan die bestanddele afgewissel het. Drie verskillende diëte is gebruik, elk waarvan 90% van een bestanddeel bevat het.

varied. Three different diets were used, each of which consisted of 90% of one component.

3. A group whose diet was stabilized on a normal (2,000 calories) daily diet. They were changed to a 2,600-calorie diet, alternatively of high-fat and high-protein composition, to see whether they lost weight in confirmation, more or less, of the results in group 2.

Although the entire experiment was neither large, nor prolonged, it appears to have been conducted with a thoroughness that makes the results noteworthy, even if they do not find general acceptance.

The results of the first series bore out the generally-accepted view that the less a person eats the faster he will lose weight. By making weekly alterations in the total daily calorie-intake of each patient, Kekwick and Pawan demonstrated a clear proportional relationship between intake and weight loss. The second series yielded more interesting results; here the total calorie-intake could still be regarded as a reducing diet (1,000 calories), yet the patients on the 90%-carbohydrate diet lost no weight at all while the losses on those on the 90%-protein and 90%-fat diets were marked. Some patients of the latter groups lost 1-1½ lb. a day. The response of patients in the third group provided confirmation of Kekwick and Pawan's thesis that—within limits—it is the substance of the diet that is important rather than the amount. By feeding with 600 calories over the 'normal' they recorded actual losses in weight in some of their patients—provided the whole diet was a high-fat or a high-protein one.

By means of biochemical checks that they carried out in these experiments Kekwick and Pawan were able to show that there was no defective absorption to account for the weight loss, nor any significant loss of carbohydrate stores or body protein. Slightly less than half the weight lost was shown to be due to loss of body water, and 50-70% to loss of body fat. The rate of water loss is greater with high-fat and high-protein diets; this fact—together with the marked variations in weight loss between the different constant-calorie diets—is taken to suggest that obese persons alter their metabolism in response to variations in the diet. Kekwick and Pawan draw no practical conclusions from their experiments, and they have been taken to task for their brevity, 7-9 days being very short periods for studying changes of weight in obesity,[3] and for their concludions over the role of body water in weight loss. From their own data the striking increase in water loss would itself account for about 70% of the weight lost with the high-protein or high-fat diets—and proportionately less therefore would be due to loss of body fat.

1. Lyon, D. M. and Dunlop, D. M. (1932): Quart. J. Med., **1**, 331.
2. Kekwick, A. and Pawan, G. L. S. (1956): Lancet, **2**, 155.
3. Hervey, G. R. (1956): *Ibid.*, **2**, 355.

3. 'n Groep wie se dieet op 'n normale (2,000 kalorieë) daaglikse dieet gestabliseer was. Hulle is oorgeplaas op 'n dieet van 2,600 kalorieë, waarvan die samestelling alternatief van 'n hoë vet- òf van 'n hoë proteïengehalte was, om te sien of hulle gewig verloor het, wat sodoende min of meer die resultate by groep 2 verkry, sou bevestig.

Alhoewel die hele eksperiment nòg groot nòg van lange duur was, skyn dit of dit met 'n deeglikheid uitgevoer was, wat die resultate opmerkingswaardig maak, al word hulle nie algemeen aanvaar nie.

Die resultate van die eerste reeks het die algemeen-aangenome mening bevestig dat, hoe minder 'n persoon eet, hoe vinniger hy gewig sal verloor. Deur elke pasiënt se totale daaglikse kalorieopname weekliks te verander, het Kekwick en Pawan gedemonstreer dat daar 'n duidelike proporsionele verwantskap tussen opname en gewigsverlies bestaan. Die tweede reeks het interessanter resultate opgelewer; hier kon die totale kalorie-opname (1,000 kalorieë) nog as 'n verslankings-dieet beskou word, tóg het die pasiënte op die 90%-koolhidraatdieet glad geen gewig verloor nie, terwyl die gewigsverliese van diegene op die 90%-proteïen- en 90%-vetdiëte, opvallend was. Sommige pasiënte in die laasgenoemde groep het 1-1½ lb. per dag verloor. Die wyse waarop pasiënte in die derde groep gereageer het, het Kekwick en Pawan se tesis bevestig dat—binne perke—dit die inhoud van die dieet, eerder as die hoeveelheid is, wat belangrik is. Deur hulle pasiënte met 600 kalorieë bó die ‚normale' te voed, het hulle werklike gewigsverliese by sommige van hulle pasiënte aangeteken—op voorwaarde dat die hele dieet van 'n hoë vet- of hoë proteïengehalte was.

Deur middel van biochemiese toetse wat hulle by hierdie eksperimente uitgevoer het, was Kekwick en Pawan in staat om aan te toon dat daar geen gebrekkige opname was om die gewigsverlies te verklaar nie, nóg was daar enige betekenisvolle verlies van koolhidraat-voorrade of liggaamsproteïene. Dit is getoon dat effens minder as die helfte van die gewig wat verloor was, aan verlies van liggaamswater, en 50%-70% aan verlies van liggaamsvet te wyte was. Die tempo van waterverlies is groter by diëte met 'n hoë vet- en hoë proteïengehalte; dit word aangeneem dat hierdie feit—tesame met die opvallende variasies van gewigsverlies tussen die verskillende kalorie-konstante diëte—suggereer dat vetsugtige persone hulle metabolisme as gevolg van variasies in die dieet verander. Kekwick en Pawan maak geen praktiese gevolgtrekking van hulle eksperimente nie, en hulle is berispe oor die kortstondigheid daarvan omdat periodes van 7-9 dae baie kort is om gewigsveranderings by vetsug te bestudeer,[3] en oor hulle gevolgtrekkings van die rol wat liggaamswater by gewigsverlies speel. Uit hulle eie gegewens is die opvallende toename in waterverlies skynbaar alleen verantwoordelik vir 70% van die gewig verloor by die diëte met 'n hoë proteïen- of hoë vetgehalte—en gewigsverlies te wyte aan verlies van liggaamsvet, sou dus proporsioneel kleiner wees.

1. Lyon, D. M. en Dunlop, D. M. (1932): Quart. J. Med., **1**, 331.
2. Kekwick, A. en Pawan, G. L. S. (1956): Lancet, **2**, 155.
3. Hervey, G. R. (1956): *Ibid.*, **2**, 355.

THE AIR-BORNE FUNGI IN JOHANNESBURG

A FIVE-YEAR SURVEY AS A BASIS FOR THE STUDY OF FUNGUS ALLERGY IN SOUTH AFRICA

DAVID ORDMAN, B.A., M.B., CH.B. (CAPE TOWN); D.P.H. (RAND)

and

K. G. ETTER, B.SC. (RAND)

The South African Institute for Medical Research, Johannesburg

It is well known that the inhalation of pollen may give rise to hay-fever in sensitive persons. The possibility that air-borne saprophytic fungi have a similar allergenic effect has long been suspected and numerous investigations have amply confirmed the fact that hypersensitivity to fungi not infrequently occurs, giving rise to bronchial asthma or other allergic respiratory conditions.

This survey was carried out with the object of obtaining qualitative and quantitative information about the fungi present in the atmosphere as a basis for the study of fungus allergy in South Africa. With such knowledge the physician is better equipped to assess the etiological factors in the allergic complaints of patients.

Fungi are universal in distribution and they appear in the atmosphere from soil and from living plants and dead vegetation. Air-borne fungi are also found in the dust, furniture, upholstery and bedding materials in the home and may be responsible for respiratory allergy in the persons living there.

Fungi grow in masses made up of mycelia or threads and also of spores, which are constant in the different fungi and characterize the varieties. Fungus spores are very small and light, the average diameter being 3-5 μ and are much smaller than pollen grains, which have a diameter of 15-40 μ.

The true fungi are divided into the following Classes: Phycomycetes (non-septate mycelium and asexual spores in a sporangium), Ascomycetes (septate mycelium, ascospores in an ascus), Basidiomycetes (septate mycelium, basidiospores on short sterigmata on the outer surface of a basidium) and Fungi imperfecti (septate mycelium, and include conidial and asexual reproduction stages of other Classes). It is interesting to observe that the great majority of the air-borne fungi fall into the Class of Fungi imperfecti, the commonest being *Acromoniella*, *Alternaria*, *Aspergillus*, *Botrytis*, *Cephalosporium*, *Cephalothecium*, *Cladosporium* (*Hormodendrum*), *Epicoccum*, *Fusarium*, *Helminthosporium*, *Paecalomyces*, *Penicillium*, *Pestalotiopsis*, *Phoma*, *Pullularia*, *Scropulariopsis*, *Sporotrichum* and *Trichoderma*. It is also in the Order Moniliales of Fungi imperfecti that the yeast-like fungi, *Monilia* and *Torula* belong. The *Ascomycetes* are represented by *Chaetomium* and some species of *Penicillium* and *Aspergillus* as well as the true yeasts. The plant parasites *Ustilago* (smuts) and *Puccinia* (rusts) belong to the Basidiomycetes, and *Mucor* and *Rhizopus* to the Phycomycetes.

Sometimes non-fruiting mycelia are obtained from the atmosphere and their identification is not possible in the absence of the characteristic spores. Such unidentified fungi are referred to as *Mycelia sterilia*.

SURVEYS IN OTHER COUNTRIES

Some of the atmospheric fungus-surveys reported from Europe and the Americas are summarized below to indicate the fungus varieties generally encountered:

Bernstein and Feinberg[1] exposed 2 plates of potato dextrose agar consecutively for 15 minutes each day in Chicago over a period of 5 years. They found that *Alternaria* contributed 30% and *Hormodendrum* (*Cladosporium*) 42% of all the spores grown. *Penicillium* and *Aspergillus* came next with 11 and 4% respectively. A large number of other fungi were found but each contributed only 3% or less of the total.

Morrow *et al.*,[2] studying the atmospheric fungus content in 9 States of the USA from the Great Lakes to the Gulf Coast, also found that *Alternaria* and *Hormodendrum* (*Cladosporium*) were encountered more frequently and occurred in higher numbers than any other mould. *Aspergillus* and *Penicillium* counts were, however, low. In a later study Morrow[3] confirmed that the commonest genera found at all stations were *Alternaria*, *Hormodendrum* (*Cladosporium*), *Penicillium*, *Aspergillus*, *Pullularia*, sterile pale species, sterile dark species, *Torula*, *Fusarium* and *Trichoderma*.

Nilsby,[4] working in Sweden, found *Hormodendrum* (*Cladosporium*), *Penicillium*, *Pullularia*, and yeast-like fungi to be the commonest air-borne fungi.

Passarelli *et al.*[5] carried out a 2-year study of the incidence of air-borne fungi in Rio de Janeiro, Brazil. Plates were exposed at weekly, and later at fortnightly, intervals for 15 minutes each time. The commonest fungi found were yeasts (30·2%), *Hormodendrum* (*Cladosporium*) (16·5%), *Rhodotorula* (16·4%), *Penicillium* (14·3%), *Aspergillus* (8·0%) and *Fusarium* (3·5%). Numerous other fungi were recovered in lesser quantities—principally *Phoma*, *Trichoderma*, *Stemphyllium* and *Alternaria*.

In a 6-months survey in Mexico, the observations being made at fortnightly intervals, Blackaller[6] found *Hormodendrum* (*Cladosporium*) to be most numerous, with lesser numbers of *Alternaria*, *Penicillium*, and *Aspergillus*.

Targow and Plunkett[7] found the following fungi in the atmosphere over a 4-year period in the Los Angeles area: *Hormodendrum* (*Cladosporium*) (53·8%), *Alternaria* (14·8%), *Actinomyces* (7·2%), *Pullularia* (3·8%), *Epicoccum* (3·6%), *Penicillium* (3·4%), *Yeasts* (3·2%), with other genera each contributing 2% or less to the total catch.

Bruskin[8] found 52 genera of air-borne fungi in the New Brunswick and New Jersey areas. The following 12 genera made up 92% of the total count in a 21-month sampling period: *Hormodendrum* (*Cladosporium*) contributed half of the total and the following genera an additional 42%, viz. *Penicillium*, *Epicoccum*, *Alternaria*, *Pullularia*, *Aspergillus*, *Stemphyllium Botrytis*, *Cylindrocarpon*, *Fusarium*, *Helminthosporium* and *Phoma*. The remaining 8% consisted of 40 additional genera.

Hyde, Richards and Williams[9] have recently summarized the findings in a 3-year survey of atmospheric mould spores in Great Britain. Nearly 100 genera were represented but 96% of the total catch, other than sterile colonies belonged to the following 11 genera only: *Cladosporium* (37·8%), *Pullularia* (10·4%), *Penicillium* (9·1%), *Epicoccum* (3·4%), *Phoma* (3·0%), *Aspergillus* (2·9%), *Botrytis* (2·7%), *Oospora* (2·6%), *Sporotrichum* (2·1%), *Alternaria* (1·0%), and *Candida* (1·6%).

It will be observed that there is a considerable uniformity in the predominant air-borne fungi, regardless of where the observations have been made.

INVESTIGATION OF AIR-BORNE FUNGI IN JOHANNESBURG

The studies of the air-borne fungi in Johannesburg were commenced in 1948 but systematic work was delayed until preliminary experiments to determine the basis of future work on the subject had been completed. The actual investigation was begun in 1950 and records have been kept since that time. This report refers to the findings in the 5-year period 1950-1954.

Johannesburg (Lat. 26° 1′ S; Long. 28° 0′ E) is an inland city of the Highveld of South Africa, 5,600 ft. above sea-level, with cold dry winters and summer

TABLE I. CLIMATE DATA OF JOHANNESBURG (1950)

	June		*December*		*Year*	
	8 *a.m.*	2 *p.m.*	8 *a.m.*	2 *p.m.*	8 *a.m.*	2 *p.m.*
Mean Barometric Pressure, m.m.	846		841		843	
Rainfall, inches	0·8		7·5		31·5	
Mean Relative Humidity, per cent.	83	37	74	52	75	43
Mean Air Temperature, °F	42·1	64·0	65·6	75·2	56·3	71·6

rainfall. Although there is no agricultural activity in a major sense there are nevertheless small farm-holdings in the periphery of Johannesburg and in many of the suburbs nearly every home possesses a large or small garden. Certain climate data pertaining to Johannesburg which may be relevant to atmospheric fungus occurrence are shown in Table I.

Methods and Materials

Four-inch diameter plates of suitable culture media were exposed to the atmosphere at 11 o'clock each morning at the top of a 3-storey building in Hospital Hill, a Northern suburb on one of the ridges overlooking the city. As far as possible plate exposures were made each working day except during rain. Experimental trials revealed that 3 minutes was the optimum exposure time. Longer exposures resulted in plates unduly overgrown. After exposure the plates were covered and left undisturbed at room temperature in the laboratory and examined after 4 or 5 days both qualitatively and quantitatively for fungus colonies. They were then observed daily in order to identify the fungi as their characteristic spores appeared. Unidentified colonies were subcultured and re-examined about 10 days later and if necessary grown on various media to encourage sporulation.

At first dextrose agar medium plates alone were used. It was soon found, however, that on this medium the colonies increased rapidly in size with a tendency to spread over large areas. There was thus the possibility that other colonies coming up subsequently might be obscured. For this reason it was decided to use in addition Littman's ox-gall agar plates, because on this medium colonies were much smaller in size, development was slower and, on account of the streptomycin in the medium, bacterial growth was inhibited. With these two media used simultaneously it was felt that a truer estimate of the atmospheric fungus content was possible. Shortly thereafter it was decided to expose 2 plates each of dextrose and Littman's medium, the catch being calculated on the average of each pair of plates.

During 1953 a plate of tomato agar medium was exposed along with the other two media. It was found that *Cladosporium*, *Alternaria*, *Rhizopus* and *Trichoderma* grew equally well on the three media. Dextrose agar medium was best for *Epicoccum*, *Phoma*, *Nigrospora*, *Stemphyllium*, *Fusarium* and *Helminthosporium*. Littman's medium was best for *Penicillium*, *Aspergillus* and *Cephalosporium*. The use of tomato agar medium was discarded as it did not reveal the presence of fungus varieties additional to those recovered on the other media employed.

During the whole period of the investigation and for many years before its commencement slides had been exposed at weekly intervals to study the pollen content of the atmosphere. There was thus also available during the period of the atmospheric fungus survey a record of the fungus elements caught on the pollen slides. These included rusts and smuts in relatively small numbers, which of course do not necessarily reflect their quantitative occurrence in the atmosphere. The slide-exposure method is in general not adequate for fungus counts because few fungus spores are identifiable by direct microscopic examination of the slides and in any event the nature of fungus elements in a non-sporing phase cannot be determined.

The culture-plate exposure method is not entirely satisfactory for atmospheric fungus studies. Any artificial medium used must of necessity be selective in that it permits the growth of some but not other varieties of fungi. Further, not every air-borne fungus grows on artificial medium and some will thus be lost in colony counts made. There are in addition, certain difficulties in regard to colony counts which must be considered: (*a*) Some fungi (e.g. *Penicillium*) rapidly produce 'daughter colonies' which must be watched for lest they be included in the count of colonies derived from the actual exposure, (*b*) some fungus genera (e.g. *Rhizopus*) overgrow other fungi, which may still be in the early stages of their development and so be overlooked in

the counts; and (*c*) some colonies remain unidentified in spite of various techniques and media used to induce sporulation.

In spite of the difficulties and inadequacies mentioned above, plate exposures at the same place and at the same time each day over a period of years provide satisfactory information for practical purposes in a comparative sense even if precise and absolute knowledge of the atmospheric fungus content is not obtained.

No attempt was made to identify air-borne fungi as to species. This may become necessary in the future if species differences in fungus allergens are proved to be important.

Atmospheric Fungus Findings in Johannesburg

The quantitative estimation of the atmospheric fungi in the survey in Johannesburg was recorded in two ways: (1) *Abundance*—the total number of colonies of each fungus appearing on the plates during the exposure days per annum, and (2) *Frequency*—the number of times each fungus appeared, irrespective of quantities, during the exposure days per annum.

The Abundance and Frequency of the specific air-borne fungi found in Johannesburg in the 5-year survey in an average of 282 exposure days *per annum* is shown

TABLE II. ANNUAL ABUNDANCE OF AIR-BORNE FUNGI IN JOHANNESBURG IN THE 5-YEAR PERIOD, 1950-1954

(Average Annual Exposure Days = 282)

Fungus	*Average Number of Colonies per Year*		
	Number	*Percent of Total*	
Cladosporium	1,058	32·5	
Alternaria	402	12·3	
Penicillium	330	10·1	
Epicoccum	329	10·1	84·3
Phoma	271	8·3	
Monilia *	202	6·2	
Torula *	152	4·7	
Rhizopus	55	1·7	
Yeasts *	55	1·7	
Nigrospora	54	1·6	
Stemphyllium	50	1·5	
Trichoderma	49	1·5	
Acrospeira	45	1·4	
Pleospora	37	1·1	
Fusarium	26	0·8	
Helminthosporium	23	0·7	
Aspergillus	23	0·7	
Mucor	13	0·4	
Cephalosporium	8	0·2	
Chaetomium	5	0·2	
Amblyospora, *Acromoniella*, *Botrytis*, *Cephalothecium*, *Cystophora*, *Diplodina*, *Macrosporangium*, *Paecalomyces*, *Pestalotiopsis*, *Periconia*, *Scropulariopsis*	26	2·1	15·7
Unidentified	41		

* Average for 4-year Period.

TABLE III. ANNUAL FREQUENCY OF AIR-BORNE FUNGI IN JOHANNESBURG IN THE 5-YEAR PERIOD, 1950-1954

Fungus	*Average Number of Days per Year on which the Fungus Appeared*	
	Number	*Percent of Exposure Days* (282)
Cladosporium	235	83·3
Alternaria	188	66·6
Penicillium	169	59·3
Phoma	139	49·3
Monilia	139	49·3
Epicoccum	105	37·2
Torula	86	30·5
Rhizopus	54	19·0
Yeasts	53	18·7
Nigrospora	50	17·7
Stemphyllium	43	15·3
Acrospeira	37	13·2
Trichoderma	32	11·4
Pleospora	25	9·9
Fusarium	23	8·1
Helminthosporium	22	7·8
Aspergillus	20	7·1
Mucor	12	4·2
Cephalosporium	7	2·5
Chaetomium	4	1·4
Other fungi (including 41 unidentified)	52	Each less than 1·0

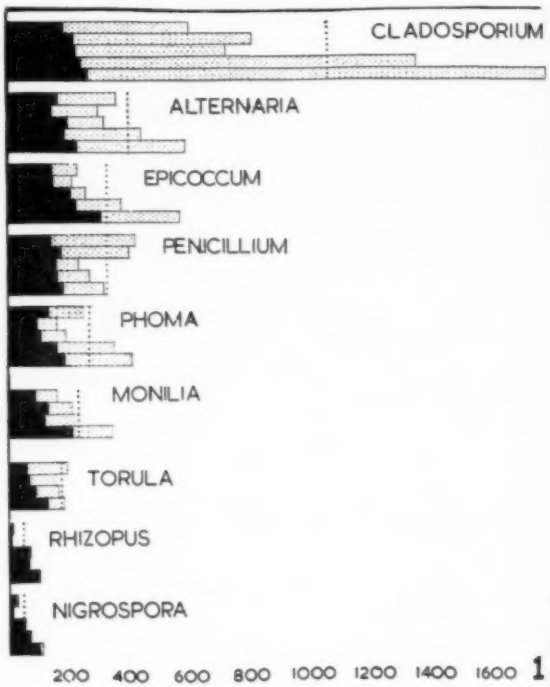

Fig. 1. The commoner air-borne fungi in Johannesburg, 1950-1954. Whole Column = *Abundance:* The total number of colonies of the specific fungus recovered in the exposure days each year. The annual average for the 5 years is shown by a dotted line. Black Column = *Frequency:* The number of days on which the specific fungus was recovered in the exposure days each year. The ratio of the whole column to the black column each year indicates the average number of colonies of the specific fungus recovered per exposure day.

in Tables II and III. It will be observed that *Cladosporium* was the most abundant fungus deposited on the plates, contributing nearly a third of all the fungi collected. The next commonest fungi were *Alternaria*, *Penicillium*, *Epicoccum* and *Phoma*, each contributing 8-13% of the total. The above 5 fungus genera together with *Monilia* and *Torula* accounted for as much as 84·3% and the remaining 15·7% was made up of 26 additional identified genera and 41 unidentified *Mycelia sterilia*. In Fig. 1 both the Abundance and Frequency of the 9 predominant air-borne fungi of Johannesburg are shown for each of the 5 years 1950-1954, the average Abundance for this period being indicated by a dotted line. The relation of the Abundance to Frequency reflects the average number of colonies of each variety of fungus found per exposure day.

It will be observed from Fig. 1 that both in Abundance and Frequency *Cladosporium*, *Alternaria*, *Penicillium*, *Phoma*, *Monilia*, *Torula* and *Rhizopus* constitute the commonest fungi in the air.

SEASONAL INCIDENCE

In many parts of the world it has been found that some of the atmospheric fungi have a seasonal incidence. Thus Hyde, Williams and Richards[9] reported that *Cladosporium*, *Pullularia*, *Epicoccum*, *Botrytis*, *Alternaria* and *Candida* had a summer predominance while *Aspergillus* and *Oospora* occurred mainly in the winter. *Phoma*, *Sporotrichosis* and *Penicillium* showed no special seasonal prevalence. In Rio de Janeiro, Passarelli, de Maranda and de Castro[5] found *Rhodotorulae* predominant in the winter and *Hormodendrum* (*Cladosporium*) commonest from the end of autumn to the beginning of spring, while the *Penicillium* incidence was lowest in the summer. No seasonal incidence was observed with *Aspergillus* and *Fusarium*. The more commonly occurring air-borne fungi in Johannesburg were similarly submitted to analysis from the point of view of seasonal occurrence. The findings are graphically shown in Fig. 2 and may be summarized as follows:

Cladosporium: Peaks of incidence have occurred in various years both in winter and in summer but there is no well-defined seasonal similarity in the 5-year period. There is however evidence of a consistent moderate rise in incidence in early summer (November).

Alternaria: No obvious seasonal incidence.

Penicillium: In some years there was a slight rise in incidence in August and November, but in general there was no significant seasonal incidence.

Epicoccum: There was generally a small rise in incidence in the Autumn (March to June) but this rise was quantitatively significant in only one of the 5 years.

SUMMARY

A survey was carried out of the air-borne fungi in Johannesburg over the 5-year period, 1950-1954.

The object of this survey was to establish a basis for the study of atmospheric fungus allergy in South Africa.

The principal genera of fungi found in the atmosphere of Johannesburg were: *Cladosporium* (32·5%), *Alternaria* (12·3%), *Penicillium* (10·1%), *Epicoccum* (10·1%), *Phoma* (8·3%), *Monilia* (6·2%), *Torula* (4·7%) and *Rhizopus*, yeasts, *Nigrospora*, *Stemphyllium*, *Trichoderma*, and *Acrospeira* (each about 1·5%).

The remaining 6·4% were constituted by 18 other fungus genera and 41 unidentified varieties.

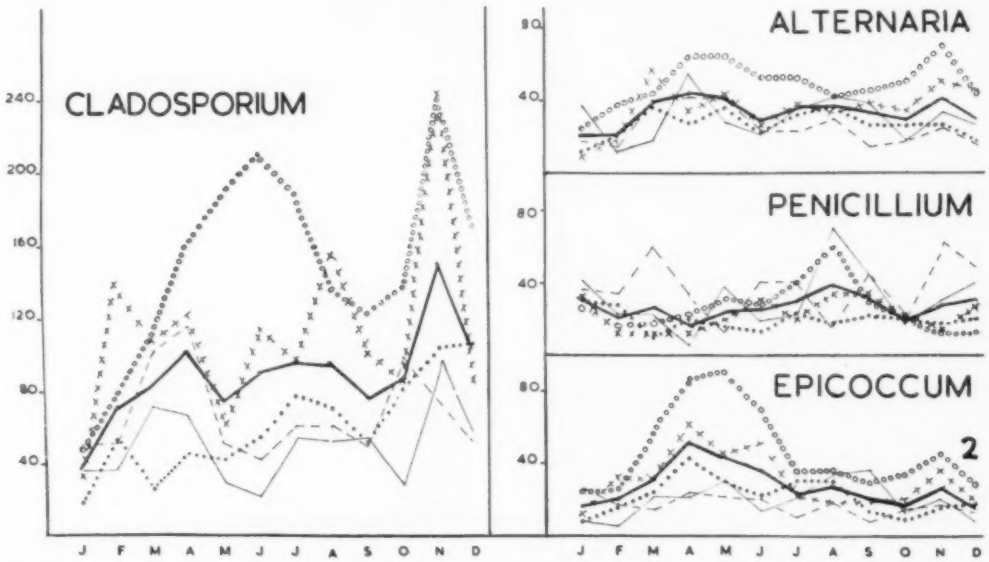

Fig. 2. Analysis of seasonal incidence of the commoner air-borne fungi of Johannesburg, 1950-1954. The total number of colonies (Abundance) of the specific fungus recovered monthly during each of the 5 successive years. The average for the 5-year period is shown by a heavy black line.

No significant seasonal incidence was noted in any of the commoner air-borne fungi.

Grateful thanks are expressed to the Director, Professor Dr. Joh. Westerdijk and Dr. G. A. de Vries of the Centraalbureau voor Schimmelcultures, Baarn, Netherlands, and more recently also to Mr. H. J. Swart of the Botany Department of the University of the Witwatersrand for their kind co-operation in the identification of some of the fungus varieties recovered. Dr. H. I. Lurie, Mycologist to the Institute, readily gave any advice sought regarding technical procedures. Acknowledgement is also made to Mr. J. de Bruijn and to Mr. M. Ulrich for assistance with the drawings and photography.

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A CONTRIBUTION TO THE VIRUS THEORY OF CANCER

W. O. FISCHER

Cancer Research Laboratory of the Hans Merensky Trust, Pretoria

In October 1950 I published in this *Journal* an article under the heading *Primary Carcinoma of the Liver in East African Natives: is it caused by an Infective Agent*[1]? Peculiar inclusion-bodies were found in cells of the anterior lobes of the hypophyses of 17 Native mine workers who died of primary carcinoma of the liver during the years 1929-39, and which were produced in the adrenals of guinea-pigs inoculated with emulsions of the affected hypophyses. The role the hypophysis and the other endocrinal glands may play in contributing to the formation of malignant growths was discussed. The results of these experiments were summarized in the article as follows:

1. In the hypophyses of 17 Native mine workers who died of primary carcinoma of the liver, intracytoplasmic inclusion-bodies were present. These bodies could not be demonstrated in Natives of the same tribes who died at the same time of other diseases.
2. In the sub-inoculated guinea-pigs and rabbits these inclusion-bodies appeared in the cytoplasm as well as in the nuclei of the host cells in various organs.
3. The nature of these inclusion bodies is not fully understood, but it is regarded as significant that they appeared in the patients as well as in the experimental animals.
4. From these preliminary observations the question arises whether these inclusion-bodies represent inclusion-bodies of a virus. More work is essential in order to establish their true nature, and to come to a conclusion whether these organisms are capable of contributing in any way to the formation of malignant tumours.

INCLUSION BODIES

In June 1951 I was able to resume my research work, which had been interrupted by the war. By kind advice of Dr. A. J. Orenstein, Dr. H. C. Berman provided me with the hypophysis of a Native mine-worker who had died of primary carcinoma of the liver with metastases in several other organs. Dr. T. Gillman—then of the Medical School Johannesburg—inoculated several guinea-pigs for me intraperitoneally with an emulsion of this hypophysis. These animals were killed 2 weeks later. In smears of their adrenals the same intracellular and extracellular bodies as described in the above article[1] were present in great numbers (Fig. 1).

I used an emulsion of the adrenals of one of these guinea-pigs for the inoculation of 7 other guinea-pigs. From these guinea-pigs a great number of passages were obtained. Again in smears of the adrenals of all the inoculated animals which were killed or died spontaneously during my experiments the same bodies could be demonstrated. The smears were stained with Azur II-Eosin, Giemsa, Victoria Blue, or Gram's method (they are Gram-negative). Up to now (31 March 1956) I have seen the bodies in the adrenals of 162 guinea-pigs, and occasionally in the ovaries and in the liver. Reference is made in the present paper to experiments on guinea-pigs only, as the tests on other animals are not yet advanced far enough.

It is remarkable that the same bodies were encountered in the adrenals of guinea-pigs into which material

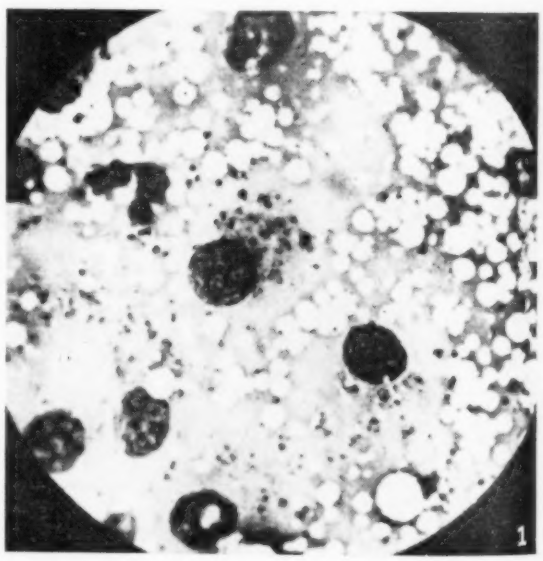

Fig. 1. Inclusion-bodies in smear of adrenals of inoculated guinea-pig (photomicrograph of this smear was published in Fig. 1 of Fischer, 1950[1]).

from a dog was inoculated which died of carcinoma of the liver with multiple metastases in other organs. They, too, were transmitted from guinea-pig to guinea-pig—altogether in 25 animals. In the previous publication[1] it was stated, that the bodies were present chiefly in the medulla of the adrenals. At that time I had examined the adrenals only in smears. But numerous histological examinations have now clearly shown that their presence is confined to the zona reticularis of the cortex.

Histopathological examinations were carried out on organs of 36 guinea-pigs inoculated with the human strain and 7 with the dog strain. The specimens were cut and stained by Mr. Gerneke at Onderstepoort. The stains used were periodic acid Schiff (PAS), haematoxylin, Giemsa, Mallory and Gram. PAS proved to be the most useful stain, with which the inclusion bodies show a bright red colour (Fig. 2). They are

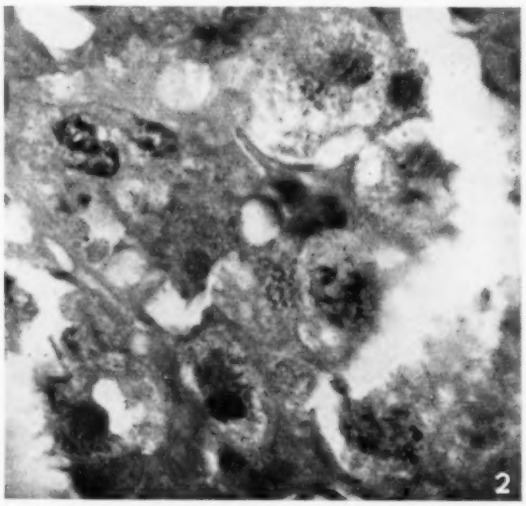

Fig. 2. Inclusion-bodies in zona reticularis of adrenal of guinea-pig inoculated with material of hypophysis of Native who died of primary carcinoma of liver.

more or less of the same appearance as described in my previous paper.[1] This was confirmed by Professor C. Jackson of Onderstepoort, who had the kindness to examine some of my specimens. He gave the following description of his findings in the adrenals of a guinea-pig the liver of which showed an early adenocarcinoma: 'Strictly confined to the deep zone (reticularis) of the cortex the epithelial cells show a spectacular content of cytoplasmic inclusion-bodies. When well developed they are often half the size of the nucleus. They are Gram-negative, react very doubtfully with Giemsa, and are strongly PAS positive. Indeed PAS is the only stain which shows them up. They look much like Negri-bodies (but the latter are not well stained with PAS). The larger ones are morulate, the smaller ones ring-like, with all apparent transitions to dust-like granules (? elementary bodies). Their relationship to material phagocytosed by the reticulo-endothelial cells of the sinusoids would need closer study, especially whether the inclusion-body material is transformed into a pigment'.

The adrenals were usually enlarged and of a somewhat firm consistence, weighing from 200 to 500 mg., whereas the weight of normal guinea-pig adrenals ranged from 90 to 150 mg. (Fig. 3). In the adrenals

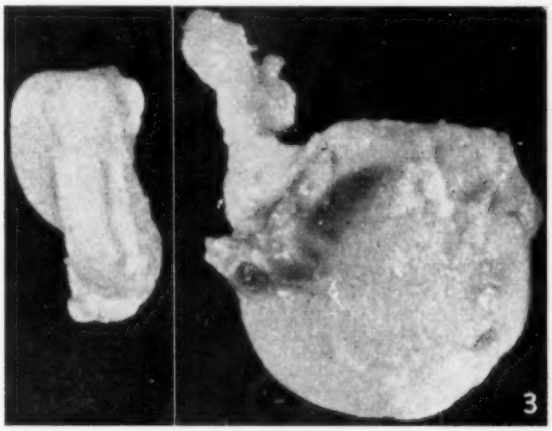

Fig. 3. Adrenals of guinea-pig. Right: heavily infected. Left: normal.

showing inclusion-bodies fatty degeneration and focal necrosis in the cortex were present.

CARCINOMA IN INOCULATED ANIMALS

In some of the inoculated animals very fine white nodules or tiny white spots were visible in the liver. In some others the surface of the organ was rough. In two animals coagulated blood was found in the abdominal cavity; the source of the bleeding could

Fig. 4. Guinea-pig. Carcinoma of liver. Killed 52 days after inoculation. 2nd passage, human strain.

not be detected. One adenocarcinoma occurred in a guinea-pig of the 5th passage killed 30 days after inoculation. In this case the surface of the right lobe of the liver was covered with layers of fibrin. In the same lobe 2 small irregularly-shaped yellow-white patches and 2 very fine white nodules were present. The gross pathological changes in another case of carcinoma of the liver are shown in Fig. 4. This guinea-pig, a third passage, was killed 52 days after inoculation. Histological examinations of the organ revealed lesions ranging from congestion to pronounced fatty degeneration and multiple focal necrobiosis and necrosis, with more or less pronounced proliferation of bile duct. In several cases the normal architecture of the liver tissue was greatly disturbed and hardly recognizable. Very severe fatty degeneration combined with acute catarrhal intra-hepatic cholangitis was the cause of death of 3 guinea-pigs which died spontaneously during the experiments. Figs. 5, 6 and 7 show photomicrographs of carcinoma of the liver occurring in guinea-pigs inoculated with the human strain. An adenoma of the bile duct was found in the liver of one guinea-pig which was killed 3 years and 80 days after inoculation (see Fig. 8). In the spleen of this animal multiple foci of necrobiosis with intensive leucocytic infiltration, hyperplasia of the lymphoid tissue, proliferation of the sinus epithelium and congestion occurred.

The pathological changes in the organs of the experimental animals as described above are suggestive of the presence of a toxic substance produced by an infectious agent, which in my opinion belongs to the virus group. It is certainly not a type of rickettsia.

Not all the characteristics of a virus, especially those concerning filterability and cultivation, have yet been established satisfactorily, owing to technical difficulties. But there are properties of the infectious agent worked with which are similar to those of a virus. Its visible manifestations are cytoplasmic inclusion-bodies and very fine granules much like elementary bodies as seen

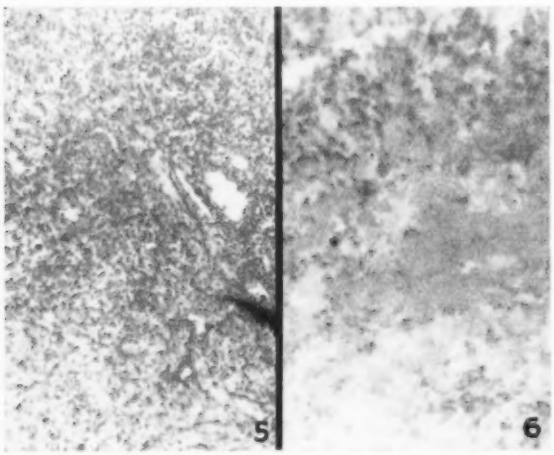

Fig. 5. Same guinea-pig as in Fig. 4. Carcinoma of liver.
Fig. 6. Same guinea-pig as in Figs. 4 and 5. Carcinoma of liver.

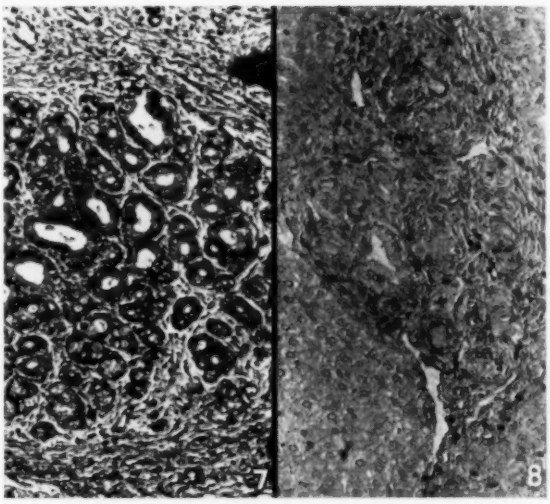

Fig. 7. Guinea-pig. Killed 27 days after inoculation. Human strain. Early adenocarcinoma of liver.
Fig. 8. Guinea-pig. Killed 3 years and 80 days after inoculation. 2nd passage, human strain. Adenoma of bile-ducts.

in other virus diseases. They can be found regularly in the zona reticularis of the adrenals of sub-inoculated guinea-pigs in any number of passages of the human strain as well as of the dog strain. Carcinoma of the liver, the disease from which the patients and the dog died from whom I obtained the material for my transmission experiments, was produced in several guinea-pigs. The virus apparently has an affinity for the glands of the endocrinal system. From a series of experiments, which are not yet completed, it seems possible to transmit the virus to certain plants.

PROTECTIVE ACTION OF SERUM FROM CANCER PATIENTS

Can this suspected virus cause cancer of the liver only, or has it any relationship with other types of cancer too? To investigate this question the following experiments were carried out: Guinea-pigs were inoculated simultaneously with sera of patients suffering from various types of cancer, together with emulsions of adrenals of guinea-pigs which contained numerous inclusion-bodies. Controls were inoculated with the adrenal emulsions alone. In 30 such experiments, carried out with the *human strain*, the animals were killed 4 weeks after inoculation. Of these experiments 6 came to a premature end owing to the death of one or the other of the animals. In 15 (62·5%) of the remaining 24 experiments inclusion-bodies did not appear in the adrenals of the animals inoculated in the manner described, whilst they were always present in the controls. The sera were obtained from 6 cases of carcinoma of the cervix, 2 of the breast, 2 of the head of the pancreas, and one each of the oesophagus, the stomach, the rectum, the colon, and the parotid gland. In the other 9 experiments (37·5%), in which the sera were obtained from 5 cases of carcinoma of the cervix, 2 of the stomach and one of the hepatic

duct, both the inoculated animals as well as the controls showed inclusion-bodies in the adrenals.

In 3 similar experiments, *with the dog strain* the sera from one case of carcinoma of the cervix, one of the breast and one of the parotid gland were combined with strongly positive adrenal emulsions of the dog strain. Inclusion-bodies could be detected in the adrenals of the controls only. These sera had also been used with the same result in some of the experiments with the human strain.

All the sera in these experiments were provided from the clinical wards of Professors L. J. te Groen and J. K. Bremer of the University of Pretoria, to whom I am greatly indebted.

In 15 of the experiments with the human strain and in the 3 with the dog strain the sera of the cancer patients had apparently lowered or neutralized the virulence of the adrenal emulsions. In 9 experiments the sera had no inhibitory effect at all. From the results of the majority of these experiments it appears that the sera of patients suffering from various types of carcinoma may contain antibodies which can adversely affect the virulence of the suspected virus.

The experiments are of a somewhat empiric character. The adrenal emulsions were taken from different guinea-pigs, because to obtain such an emulsion the animal had to be killed. A few sera only were obtainable on any one day. Therefore no more than 2-4 sera could be combined with the same emulsion. Furthermore the content of antibodies in the sera must have varied considerably, as it depends on the stage and duration of the disease. In old-standing cases a weak content only or none at all can be expected. Accurate data in this regard were not always obtainable.

These experiments, which were of a preliminary nature, gave rise to more extensive research in the serological field, which is still proceeding. More work is essential in order to arrive at definite conclusions.

CONCLUSION

The interpretation of cancer as a virus disease would imply that it is not a disease affecting certain organs only, but an infection of the whole body. The virus may enter the body in similar ways to the germs of other virus diseases. It may be harboured by healthy individuals, remaining harmless as long as the resistance of the tissues is not lowered—for instance by other diseases, malnutrition or old age. The early manifestations of the infection may be so slight and insignificant that they are easily overlooked or confounded with other conditions, inasmuch as in this stage full recovery may take place. Otherwise malignant growths may occur as a late symptom after the virus has invaded the hypophysis and other glands of the endocrinal system, upsetting their normal function.

SUMMARY

1. A description is given of the results of numerous transmission experiments carried out with material obtained from the hypophysis of 18 Bantu mine workers who died from primary carcinoma of the liver, and from a dog which died from carcinoma of several organs.

2. These observations suggest that this material contained an infectious agent of the virus group.

3. Visible manifestations of this suspected virus—inclusion-bodies—could be demonstrated in the adrenals of sub-inoculated guinea-pigs—human strain and dog strain alike—in many passages.

4. In several of these guinea-pigs true carcinoma of the liver was produced. In some others pathological changes were observed in the liver and in the adrenals suggestive of beginning malignancy. The lesions found in the organs of all the inoculated guinea-pigs are attributed to the presence of a toxic substance.

5. It appears that a relationship exists between this suspected virus and at least some of the other types of carcinoma.

I wish to express my gratitude to all the gentlemen already mentioned. Thanks are also due to Prof. J. Barnetson, Director of the Institute of Pathology of the University of Pretoria, for the many facilities placed at the disposal of the Cancer Research Laboratory of the Hans Merensky Trust. I am greatly obliged to Dr. W. K. Dannheimer for the numerous photomicrographs. Copies and enlargements of them, and the photograph of the gross specimen of the liver, were made by Mr. G. O. Kirsten.

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INTERNAL CAROTID ARTERY THROMBOSIS

A CASE REPORT

N. McE. LAMONT, M.D. (GLASG.), F.R.F.P.S.

and

D. BRINK, M.B., CH.B. (CAPE TOWN), D.M.R.D. (LOND.)

King Edward VIII Hospital, Durban

It was in 1937 that Moniz[1] first reported angiographic studies in carotid-artery thrombosis, thereby focussing attention on this rare condition. We report this case in detail as it has presented with certain unusual features.

CASE REPORT

An African Pondo male, aged approximately 40 years, was working on 6 April 1956, when he complained of headache. The next day he had a right-sided Jacksonian seizure, which was witnessed by the medical officer of the sugar company for which the patient worked as a cane-cutter. On the following day he was paralysed on the right side of his body, and was noticed to have a speech defect. He was admitted on the next day (9 April) to this hospital.

Examination showed the patient to be in a drowsy state and completely inarticulate. The *dysphasia* seemed more motor than sensory in that he appeared to understand commands, but failed to respond correctly. He was incontinent of urine but there were no signs of retention. His first bowel-action took place 5 days after admission with the aid of an enema. He showed no signs of distress and was not restless.

Nervous System

A detailed examination of the nervous system showed the following positive findings (the examination was completely objective on account of the dysphasia):

Cranial Nerve II. (*a*) *Visual Fields.* Accurate assessment in the early stages was not possible, but later examination failed to reveal any hemianopia. It was, however, suspected that the vision of the left eye was impaired at the original examination. (*b*) *Fundi.* There was distinct papilloedema of the left optic disc. The veins were engorged, but there were no haemorrhages. The right fundus was normal. These findings changed after the patient had been in hospital for 5 days, shortly after an arteriogram was performed. Marked pallor of the left retina, a pale disc, a few poorly-filled vessels, and a cherry-red spot at the macula were found. The picture was in fact one of complete occlusion of the central artery of the retina. On 25 May, 6 weeks later, examination showed the fundus of the right eye to be normal, and confrontation showed no apparent sectorial field loss. The left eye had the appearance of an old occlusion of the central artery of the retina with attenuated vessels, optic atrophy, and haemorrhagic residues at the macula.

III, IV, VI. The left pupil was slightly larger than the right, and contracted only when light was shone in the right eye. Eye movements were normal, but there was a transient deviation to the right side for the first 4 days.

V. Both motor and sensory branches seemed intact, and the conjunctival reflex was present in both eyes.

VII. An upper-motor-neurone lesion of the right side of the face was evident.

IX, X, XI, XII. The patient fed well without any nasal regurgitation, and there was no deviation of the protruded tongue.

Motor System. Muscle tone was increased on the right side of the body, which was totally paralysed.

Sensory System. Pain was the only sensation assessable, and protest was elicited to pin-prick on the face, trunk, arms and legs on each side of the body.

The *reflexes* were those of an upper-motor-neurone lesion of the right side of the body.

Cerebrospinal Fluid. The pressure was 45 mm. of water, and the globulin was slightly increased. There were 6 erythrocytes per c.mm. Chlorides—710 mg.% (as NaCl); Protein—110 mg.%.

Other Findings

All *pulses* were palpable. The left carotid pulse at the level of the angle of the jaw was, however, appreciably more difficult to feel than the right.

The *blood pressure* was 110/70 mm. Hg.

The *liver* was palpable 1 inch below the costal margin in the mid-clavicular line, and was of firm consistency.

Blood Examination. Haemoglobin 13·2 g.% (89%); P.C.V. 39%; M.C.H.C. 34%. W.B.C. 7,000 per c.mm. (P. 58%; L. 34%; M. 4%; E. 4%). The blood Wassermann reaction was positive in 4 dilutions. Alkaline phosphatase 9 K.A. units. Zinc turbidity 14 units. Total proteins 7·0 g.% (albumin 3·2 g.%, globulin 3·8 g.%), A/G ratio 0·8 : 1. Cephalin cholesterol—24 hours ++, 48 hours +++.

Liver Biopsy. A good core of tissue was obtained from the right lobe of the liver (Figs. 1 and 2). This showed a mild degree of

Fig. 1. Appearances of liver biopsy showing lobular distortion producing 'scalloping' of the borders of the biopsy specimen and thickening of the portal tracts loaded with iron-containing phagocytes. × 23.

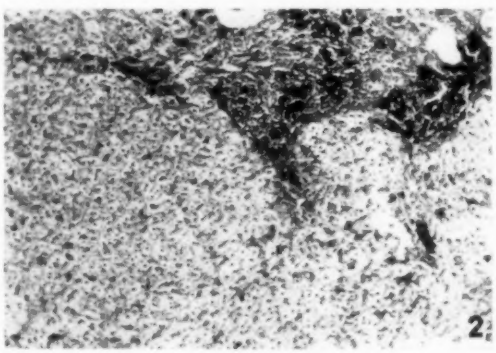

Fig. 2. Higher-power view of complete portal tract (right of centre in Fig. 1), showing coarse granular iron pigment in portal tract with stellate processes of fibrous tissue radiating from this portal tract. × 150.

hepatocellular fat and siderosis, with a moderate degree of portal siderosis. Architectural distortion was evident. The appearance was one of early cirrhosis of the liver with nutritional siderosis.

X-ray of chest showed no abnormal shadows.

Arteriography (12 April). Under local anaesthesia, the left carotid artery was punctured percutaneously by means of the Seldinger technique. The preliminary palpation established that

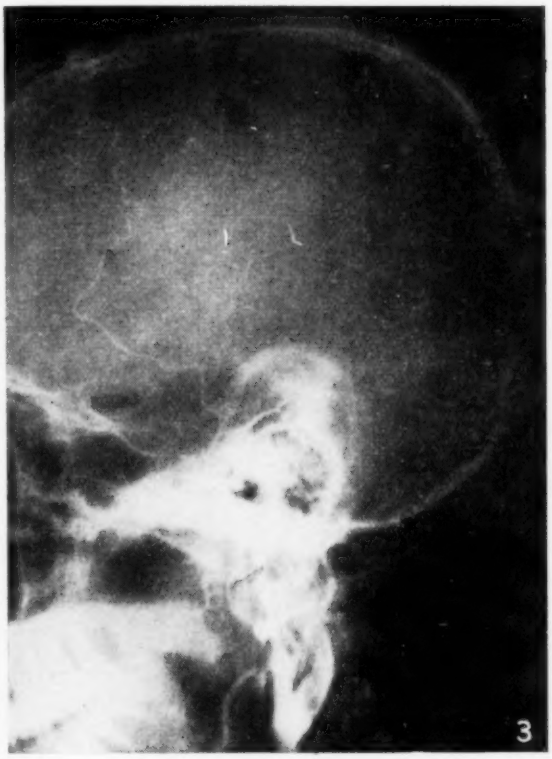

Fig. 3. Arteriogram showing occlusion of internal carotid artery close to its origin.

the artery was rather cord-like, with appreciable diminution in pulsation as compared with the right. The first injection of dye (Diaginal 40%) produced filling of the external carotid artery only, and it was thought that the catheter had possibly entered the external carotid artery. The catheter was slightly withdrawn and the tube centred down to include the neck. On repeat injection, a well-defined block of the internal carotid artery just beyond the bifurcation was demonstrated. Filling was absent beyond this point. (See Fig. 3).

Progress

During 7 weeks' observation in hospital, the patient became less drowsy, and his vocabulary increased to 4 words. Whereas at the beginning he was rather vegetable-like in his behaviour, he subsequently became emotionally labile, with occasional violent outbursts.

Treatment

As a prophylaxis against pulmonary infection, a 10 days' course of penicillin was given at the beginning of hospitalization. Apart from physiotherapy, no other active measure was employed. Anti-coagulants were not used.

DISCUSSION

The distinctive features of this case were the sudden onset of right-sided hemiplegia and dysphasia (implying involvement of that part of the brain supplied by the middle cerebral artery), together with ipsilateral papilloedema, which changed after 5 days to complete occlusion of the central artery of the retina. The latter artery is a branch of the ophthalmic artery, which rises from the internal carotid between the carotid bifurcation and the carotid syphon. It follows that those cases with the occlusion in the region of the carotid syphon will not present local eye signs, whereas those cases with the block near the bifurcation are liable to develop ipsilateral eye signs.

There is an effective anastomosis between the ophthalmic and external carotid arteries. It would appear that in the case we have presented, this anastomosis was functioning initially. Ralph[2] mentions that in cases of carotid artery thrombosis cerebral oedema occurs initially, followed by cerebral atrophy and dilatation of the lateral ventricle. This has been shown in ventriculographic studies. The initial cerebral oedema and resultant venous occlusion, together with the anastomosis between the ophthalmic and external carotid arteries mentioned above, would account for the development of papilloedema in the left eye in the case we have described.

Ralph also draws attention to the fact that filling of the anterior, and less commonly the middle, cerebral arteries of the affected side takes place when dye is injected into the opposite (patent) carotid artery. This 'cross-filling' takes place *via* the anterior communicating artery in the circle of Willis. The major effect of the internal-carotid thrombosis is therefore manifest most often upon the territory supplied by the middle cerebral artery.

It may be significant that the occlusion of the central artery of the retina developed shortly after arteriography (the arteriogram was done on 12 April, and the occlusion appeared on 13 April). Vascular spasm, a feature common during arteriography, may have caused the final sealing off of the anastomotic blood-supply to the left eye. This must have been precarious, as shown by the functional interruption of the pathway of the light reflex which was found at the first examination. This raises the question whether the intra-arterial injection of vasodilator drugs such as procaine before the injection of contrast medium should be undertaken as a routine measure in cerebral arteriography.

Ralph points out that the procedure of 'cross-filling' has been attended by a fatal outcome in 4 reported cases, and he stresses the inadvisability of its use as a routine diagnostic procedure.

The symptomatology in 107 reported cases of thrombosis of the internal carotid artery has been reviewed by Johnson and Walker.[3] According to their analysis, the case we have described would appear to fall into the group characterized by sudden catastrophic onset (35% of the 107 cases). The other main groups were those with a slowly progressive course (25%), and those with transient attacks (40%). Papilloedema was recorded in only 2 cases of the 107 reported. There was no case mentioned with initial papilloedema followed by occlusion of the central artery, nor was consensual contraction to light of the pupil recorded. A positive serological reaction for syphilis was found in only 2 cases in the analysis.

The angiographic picture of the occlusion (Fig. 3) differs in outline from the types described by Gurdjian and Webster[4] (Fig. 4). They record none in which the block was convex downwards. We can only assume that

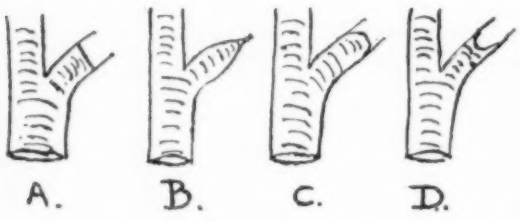

Fig. 4. Diagram showing common forms of occlusion[4] A, B and C, as compared with D found in this case.

the unusual shape was due to the fact that the arteriogram was done at an early stage in the development of the occlusion.

The organic liver-disorder in this case may be co-incidental. It is interesting, however, to conjecture the possibility of an aetiological relationship. There is evidence to suggest that the macromolecular syndrome in chronic malnutrition (Gillman and Gillman[5]), is associated with cardiovascular and other forms of fibrosis. Fisher[6] considers that the commonest cause of thrombosis of the carotid artery is atherosclerosis. Syphilis must also be considered as a possible aetiological factor in this case, bearing in mind that liver cirrhosis is sometimes associated with a false positive serological reaction.

SUMMARY

A case of spontaneous thrombosis of the left internal carotid artery, diagnosed by angiography and associated with nutritional siderosis and cirrhosis of the liver, is described. Certain unusual features are discussed with reference to the literature.

We record our thanks to Dr. Disler, Superintendent of King Edward VIII Hospital for permission to publish this case; to Dr. I. C. MacEwan for confirmation of the ophthalmology, and to Prof. T. Gillman for the report on the liver biopsy and also for his constructive criticism.

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STUPOR IN INFANTS FOLLOWING THE USE OF NASAL DROPS

A CASE REPORT

FRANK WALT, M.R.C.S., L.R.C.P., D.C.H. (ENG.)

and

LIONEL SAVAGE, M.B., B.CH. (RAND)

Durban

Young infants frequently snuffle because of nose blockage; it may be the result of coryza, regurgitation of milk through the nose, or excessive production of mucus. This interferes with satisfactory feeding and when relief is sought by the mother nasal drops are often prescribed. To-day nasal preparations are included in the flood of modern advertising and salesmanship which is directed at the doctors through pamphlets, booklets and free samples, and it is not always easy to resist these invitations to be in the vanguard of modern therapy. Here we report a case in which the use of Tyzine hydrochloride was followed by marked somnolence and respiratory and depression.

CASE REPORT

M.C. was delivered by Caesarean section on 22 May 1956 in the 35th week of pregnancy because haemorrhage had resulted from placenta praevia; labour had begun 12 hours previously. The infant was blue at birth but satisfactory respiration was established within 20 minutes after aspiration of the mucus from the mouth and stomach contents and the administration of gastric oxygen. Apart from 2 cyanotic attacks the infant progressed satisfactorily; when first weighed at 48 hours after birth he was 3 lb. 6 oz. On discharge at the age of 1 month he was sucking well at the breast at 4-hourly intervals and weighed 4 lb. 1 oz.

At the age of 5 weeks he developed a 'cold' with a blocked nose which caused much difficulty when breast feeding and Tyzine hydrochloride (0·1%) nose drops diluted to 1 in 4 (0·025%) were prescribed, one drop to be instilled into each nostril every 4 hours before feeds. The drops were first used at the 6 p.m. and 10 p.m. feeds on 26 June 1956 and again at midnight because the baby became very restless and irritable and cried; he refused to feed, his breathing remaining noisy. Four hours later drops were again inserted but the baby could not be roused to take a feed and was allowed to sleep until 10 a.m., when drops were used once more. By this time at least 10 drops (and probably more) had been used and the baby remained very somnolent and refused to suck altogether. At 3 p.m., 21 hours after the commencement of the therapy, he was found to be stuporose and pale with gasping and shallow respirations; the pulse rate was 100 per minute and he could not be roused at all. Physical examination did not reveal any localizing signs of infection or other signs of disease and it was concluded that the nose drops were to blame. Nikethamide B.P., ½ c.c., was injected subcutaneously and within 10 minutes the infant had been roused enough for him to begin sucking and take a 3-ounce feed. Thereafter he once more relapsed into a stupor and could not be roused sufficiently for his next feed. At 8 p.m., 10 hours after the drops had last been used, the irregular and gasping respirations were still present, the pulse was 80 per minute, he was pale, and the extremities were cold. He could be roused,

however, by flicking the sole of the foot, which produced a good cry. Because of this he was not disturbed until 2 hours later, when he sucked 2 ounces of expressed breast-milk fairly well. Later he took a further feed and by next morning was quite normal again and eager to feed at the breast.

DISCUSSION

Tyzine hydrochloride has recently been marketed in this country in a 0·1% solution for the relief of nasal congestion by its vasoconstrictive action. On the container it is stated that a weaker solution (0·05%) should be used for infants and children under 6 years of age. The suggested dosage is 1-2 drops for infants and 2-3 drops for young children every 4-6 hours.

From the experience with our case it is suggested that this dosage is too high, especially in view of the difficulty of measuring and instilling one or two drops accurately; it is felt that these drugs should never be used for infants. Other substances such as Privine hydrochloride and ephedrine hydrochloride have also caused drowsiness and marked sedation in infancy (Waring 1945).

Recently Brainerd and Olmsted (1956) reported 3 cases of drowsiness and lethargy in infants following upon the use of Tyzine. They carried out experiments on 19 other infants by administering nasal drops for a period of 1-4 days. Of 25 tests, all in babies under the age of 1 year, 10 produced moderate or severe drowsiness. The severe reactions occurred in those under 6 months.

Neither Parish (1954) nor Menger (1955) reported any ill effects from the use of Tyzine in their cases.

SUMMARY

A case of severe stupor caused by the use of Tyzine-hydrochloride nasal drops in a premature infant is reported. It is felt that drugs such as Tyzine and Privine should not be used in infants under one year of age.

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UNIVERSITY OF THE WITWATERSRAND

Dr. J. F. Murray, Medical Superintendent of the Diagnostic Department of the South African Institute for Medical Research, has been appointed Honorary Professor of Clinical Pathology in the Department of Pathology and Microbiology. He assumed duty on 1 September 1956.

Prof. J. F. Murray

Professor Murray, who is an authority on haematology, is a Fellow of the International Society of Haematology, to which body he was elected in 1948. He has been a member of the Institute for Medical Research since 1937 and was appointed Medical Superintendent in 1951.

Born in Scotland, Professor Murray went to Canada at an early age, but he returned to Dundee at the age of 16 and, after matriculating at the Harris Academy there, became a student at St. Andrew's University, where he graduated with the degree of M.B., Ch.B. After serving his housemanship at the Dundee Royal Infirmary he became a junior lecturer and later a senior lecturer in the Department of Bacteriology at the St. Andrew's University. In 1935 he received the degree of Doctor of Medicine and for his thesis on bacteriology he was awarded the Rutherford Gold Medal. He also holds the D.P.H. (St. Andrew's).

In 1935 Professor Murray left for Bechuanaland where he practised for 2 years. In 1937 he joined the staff of the Institute for Medical Research as bacteriologist and later was in charge of haematology for several years. He was appointed senior pathologist in 1947.

Professor Murray is medical consultant for Southern Africa to the World Health Organization and from 1953 to 1955 he directed a research programme into treponematoses in Bechuanaland on behalf of WHO. He reported his findings at the second international WHO conference on yaws in Nigeria last year. He is a member of the Dental and Medical Committee of the Council for Scientific and Industrial Research.

A former member of the Johannesburg General Hospital Board, he visited Britain in 1951 where he spent some time studying administrative methods in various research and medical laboratories.

Dr. J. W. H. Hovy

Dr. Hovy has been appointed Lecturer in the Department of Pharmacology and Therapeutics.

He was born in Holland and matriculated at Velzen in 1930 with first-class passes in physics, chemistry, mathematics and biology. In 1934, he graduated as 'Biologisch Candidaat' at the State University at Utrecht. He continued with his studies at the University of Utrecht until 1936, when he was awarded a bursary for postgraduate studies at the University of Pretoria.

Dr. Hovy then went to Rhodesia, where he held the position of Government Research Officer at the Tobacco Research Station at Trelawney, Southern Rhodesia. He returned to the Union and from 1939 to 1945 worked in a similar capacity at the Central Tobacco Research Station at Kroondal, near Rustenburg. He received the degree of Ph.D. in 1950.

Dr. Hovy went to Europe in 1955 and spent 6 months at the Physiological Institute at the University of Berne, Switzerland. He visited the Zoological Institute and the Rockefeller Institute of Physiological Research at Utrecht, Holland. He attended the Congress of the British Society of Experimental Biology in Groningen and the Congress of Swiss Physiologists and Pharmacologists at Lausanne.

The author of numerous publications, Dr. Hovy has for several years been an external examiner for the South African Pharmacy Board.

Dr. P. V. Tobias

Dr. Tobias, Senior Lecturer, Department of Anatomy, returned to the University in August 1956, after an absence of 20 months in Europe and America.

As a Nuffield Dominions Senior Travelling Fellow, he spent a year at Cambridge, carrying out research in the Duckworth Laboratory of Physical Anthropology. He also worked on fossil man at the British Museum (Natural History), South Kensington, and spent periods at various London medical schools, Oxford and Edinburgh. He attended the 6th International Anatomical Congress in Paris in July 1955, and officially represented the South African Association for the Advancement of Science at the annual meeting of the British Association at Bristol in August-September 1955. As holder of a Rockefeller Travel Grant, Dr. Tobias went to the United States for 6 months and visited various institutions throughout the country.

Dr. Tobias has been elected a Fellow of the Royal Anthropological Institute of Great Britain and Ireland.

Prof. J. Gillman

Professor Gillman, Head of the Department of Physiology, left for Europe in June 1956, to attend a series of international conferences on cancer. He attended meetings of the Physiological Society of the United Kingdom in London and the International Physiological Congress in Brussels, and discussed developments in a research project he is undertaking with authorities in Basle, Switzerland.

In August he attended a meeting of the executive committee

of the International Union Against Cancer in Rome and later was present at a meeting of the Programme Committee to draw up details for an international congress on cancer to be held in London in 1958.

On his way back, in September 1956, Professor Gillman attended a conference on liver cancer in Kampala, Uganda, and another conference in Leopoldville, Belgian Congo.

Other Appointments

Prof. O. S. Heyns, Head of the Department of Obstetrics and Gynaecology, has been appointed Dean of the Faculty of Medicine.

Dr. A. D. Bensusan has been appointed part-time Director of the Photographic Unit of the Department of Medicine as from 1 July 1956. Dr. Bensusan is a Fellow of the Royal Photographic Society of Great Britain, a Fellow of the Royal Society of Artists, a Fellow of the Photographic Society of America, a member of the Biological Photographic Association of America, and founder and president of the Photographic Society of Southern Africa.

Dr. S. Cohen, Senior Clinical Lecturer and Senior Dental Surgeon, Oral and Dental Hospital, has been appointed Leverhulme Research Fellow in Oral Pathology at the Royal College of Surgeons of England. He has resigned from the service of the University as from 31 December 1956.

Dr. J. A. Douglas has been appointed Acting Head of the Department of Surgery, *vice* Professor W. E. Underwood, who resigned as from 31 August 1956.

Professor J. T. Irving, Director of the Dental Research Unit of the University and the South African Council for Scientific and Industrial Research, returned to Johannesburg in August 1956 from Europe, where he attended the International Physiological Congress in Brussels and a conference on Dental Caries in London. Professor Irving also visited America where he carried out research in the Department of Oral Histology at the University of California.

Dr. F. Daubenton, Senior Obstetrician and Gynaecologist and senior assistant to the Professor in the Department of Obstetrics and Gynaecology, who is second in command, with the rank of Major, of No. 5 Field Ambulance, S.A. Medical Corps, A.C.F., received the John Chard Medal from the Surgeon-General at a parade in Pretoria in August 1956.

Prof. G. A. Elliott has been re-appointed to represent the University on the Leprosy Advisory Committee for a further 5 years as from 1 September 1956.

Dr. L. F. Freed, Honorary Lecturer, Department of Sociology and Social Work, has accepted an invitation to attend an international conference on Prostitution, which has been organized by the International Abolitionist Federation of Geneva at Frankfurt-am-Main, in October 1956.

Dr. P. B. Peacock, Senior Lecturer, Department of Preventive Medicine, has resigned as from 31 August 1956. He has been re-appointed in a part-time capacity.

NEW PREPARATIONS AND APPLIANCES : NUWE PREPARATE EN TOESTELLE

Tyzine Pediatric Nasal Drops. Pfizer's Tyzine nasal decongestant is now available in a new concentration (0·05%) specifically for infants and children, in a ½ oz. dropper bottle. The manufacturers supply the following information:

Tyzine Pediatric maintains all the properties of 'normal' Tyzine. A notable feature is the special pack—the calibrated dropper is designed to ensure easy and precise dosage in the youngest patient and to assist the mother to give the prescribed dose correctly. The dropper is made of polythene to avoid damage to the mucous membrane. The pink colour makes a special appeal to children.

Indications. Inflammatory hyperemia and oedema of the nasal mucosa and congestive obstruction of sinus and eustachian ostia, as may occur in the common cold, hay fever, vasomotor rhinitis, chronic hypertrophic rhinitis and sinusitis. Its use is adjunctive to any anti-allergic, anti-infective, or surgical measures that are indicated.

Dosage and Administration. 2-6 years—1-2 drops Instilled into each nostril not more often than 4-hourly. Under 2 years—1 drop in each nostril 4-6 hourly.

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Veroxil: A New Vermifuge. The Crookes Laboratories have recently introduced Veroxil Elixir and supply the following information. The Elixir contains the equivalent of 0·5 g. of piperazine hydrate in each teaspoonful (4 ml.) and provides an elegant, acceptable and simple means of administering the drug.

The discovery of the vermifugal activity of the salts of piparizine constitutes an important advance in the management of oxyuriasis and ascariasis. Piparizine is well tolerated and easy to administer, and secondary measures, other than careful attention to personal hygiene, are unnecessary. By its use threadworm infestation can be eliminated in 7 days and roundworm infestation can be treated with a single dose. Side-effects, which include blurring of vision, muscular incoordination and vomiting, are transient and are usually due to over-dosage. These reactions soon subside if treatment is stopped, and are rare when the correct dosage is used.

Single-dose treatment—ascariasis only: Adults and children over 42 lb., 6 teaspoonfuls; infants and children under 42 lb., 4 teaspoonfuls; preferably before the evening meal.

Seven-day treatment—oxyuriasis and ascariasis—varies considerably according to age (see literature), e.g. 9 months ½ teaspoonful twice a day, 14 years 2 teaspoonsful twice a day.

Veroxil Elixir is packed in 4 oz. bottles. Detailed literature and clinical samples are available from P.O. Box 1573, Johannesburg.

PASSING EVENTS : IN DIE VERBYGAAN

Mr. Ralph Ger, F.R.C.S., F.R.C.S.E., has commenced practice as a specialist surgeon in Cape Town. Telephones: residence 7-9705, rooms (temporary) 2-3649.

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National Research Council of Canada: Postdoctorate Fellowships. Fellowships will be awarded for 1957-58 by the National Research Council, tenable in various Canadian laboratories. Applicants should not be more than 35 years old and should possess a Ph.D. degree or expect to obtain it before taking up an award. Annual stipend $3,700 for single Fellows and $4 500 for married (male) Fellows, with travelling grants both ways (including grant towards wife's travelling). Fellowships will be awarded for initial terms of one year, and renewal for a second year will be considered. Applications to be made on special forms obtainable from Awards Office, National Research Council, Ottawa, Canada, or Chief Scientific Liaison Officer, National Research Council of Canada, Africa House, Kingsway, London, W.C. 2, and to be received in Ottawa not later than 15 February 1957. Booklets describing the fields in which Fellowships are available are obtainable from the Awards Officer, National Research Council, Ottawa, to whom inquiries may be directed.—*C.S.I.R.*

* * *

Association of Surgeons. The Annual Meeting of the Association of Surgeons of Great Britain and Ireland, to which members of the Association of Surgeons of South Africa are invited, will be held on 25, 26 and 27 April 1957 at Newcastle-upon-Tyne. Discussions will take place on *Prevention of Sepsis in Theatres and Wards* (Prof. L. P. Garrod and Dr. R. Blowers), *Minor Complaints of the Rectum and Anus* (chairman, Mr. C. Nauton Morgan), *Dupuytren's Contracture* (Mr, Fenton Braithwaite and Mr. Harold Bolton),

The Early Treatment of Burns (Mr. A. B. Wallace), and *Thyrotoxicosis* (Mr. K. Paterson-Brown and Dr. Robert Trotter). Other events include short papers, the Rutherford Morison Lecture, the Business Meeting, operating sessions and demonstrations, visits to places of historical and cultural interest, reception by the University of Durham, and the Annual Dinner. As stated above, members of the Association of Surgeons of South Africa, which is affiliated with the above Association, are entitled to attend.

* * *

Whooping Cough made Notifiable in Simonstown, C.P. In Government Notice No. 1877 of 19 October 1956 it is announced that the Minister of Health has declared whooping cough to be a notifiable disease within the municipal area of Simonstown.

* * *

Research Forum, University of Cape Town. At the meeting of the Research Forum which, as previously announced, will be held on Tuesday 6 November 1956 in the A-Floor Lecture Theatre, Groote Schuur Hospital, Cape Town, at 12 noon, Dr. J. B. Herman will not be the speaker. His place will be taken by Dr. W. P. U. Jackson and Dr. N. Woolf, who will speak on *Pre-diabetes—its ramifications and diagnosis.*

* * *

2nd International Congress for Social Medicine, Vienna. The Austrian Scientific Society for Social Medicine is arranging the next international congress in Vienna from 31 May to 2 June 1957, under the auspices of the International Society for Hygiene and Prophylactic Medicine. The theme of the congress is *University and Public Health*—the Place and Task of the University. It is intended to have only brief lectures and devote most time to discussions. Requests and proposals should be addressed to Prof. Dr. T. Antoine, Spitalgasse 23, Vienna 9, Austria.

* * *

Dispensing by Doctors. Speaking at a meeting at East London on 24 October, the Minister of Health, Hon. J. H. Viljoen, in reply to an enquiry on the subject, is reported to have said that there was little chance of prohibiting doctors and dentists from dispensing medicines until some agreement was reached between chemists and the medical profession. The preventing of doctors from dispensing medicines might cause great hardship for patients in the lower income group.

* * *

Witwatersrand Medical Library. During December 1956 extensive alterations will be made to the plumbing in the Medical School. From the 3rd to about the 24th, working conditions in the Medical Library will be very disturbed, borrowers are advised to make their enquiries and requests by telephone, confining their visits to the Library to the time between 5 p.m. and 6 p.m. daily, after the workmen have left.

REVIEWS OF BOOKS : BOEKRESENSIES

YEAR BOOK OF DERMATOLOGY AND SYPHILOLOGY

The Year Book of Dermatology and Syphilology 1955-1956 *Series.* Edited by Rudolf L. Baer, M.D. and Victor H. Witten, M.D. Pp. 480. 61 Figures. Chicago: The Year Book Publishers, Inc. 1956.

Contents: Introduction. Selected Aspects of Dermatologic Therapy with Superficial X-rays and Grenz Rays. 1. Treatment and Prevention. A. Endocrine Therapy. B. Physical Therapy. C. Other Therapy. 2. Eczematous Dermatitis, Atopic Dermatitis and Urticaria; Allergy. 3. Drug Eruptions. 4. Miscellaneous Dermatoses. 5. Cancers; Precanceroses; Other Tumours. 6. Fungous Infections. 7. Other Infections; Infestations. 8. Venereal Diseases and Their Treatment (Exclusive of Gonorrhea). 9. Investigative Studies. 10. Miscellaneous Topics.

This is the first edition of this notable and instructive work to be published without the distinguished guidance of Dr. Marion B. Sulzberger, and there are many who will regret his departure and miss his editorial judgment. It still remains, however, an informative volume covering such a wide field that one must admire the diligence and analytical skill of the two present editors in reading such a vast amount of literature and summarizing it for our benefit.

Like year-books this is a survey of the year's work in a special field; and to review a review is a difficult matter. The specialist will no doubt form his own opinion. But for the benefit of the general reader a few points, taken at random, may be stressed.

Many articles are presented on the use of adrenal steroid preparations in various skin conditions, even when the aetiology is obscure. The remarkable beneficial effect of these medicaments on many dermatoses is undeniable. Nevertheless, caution should be observed, for ill effects from the absorption of fluro-hydrocortisone compounds are recorded. On the other hand, it appears, hydrocortisone may be used as an external application, even over long periods, without ill effect.

Encouraging results in generalized dermatoses have been obtained by workers in Germany by radiation with soft X-rays over large areas of the body. New, but potentially dangerous, substances for the chemotherapy of psoriasis, the value of Isoniazid in skin tuberculosis, and the value of hormone treatment in selected cases of acne vulgaris, are but a few of the many subjects of general interest reviewed. Those who are accustomed to read the special literature will meet many articles they have read before, but many, too, that they haven't, especially from foreign sources.

Here and there, interspersed throughout the book, the editors add little comments of their own, appraising the value of some particular investigation. These observations are usually shrewd and to the point. They prove that the editors' labours have not been a mere mechanical process of digestion. Indeed, they present us with tit-bits of well assimilated material.

If any are left who still believe that the speciality of dermatology consists in applying external remedies, chosen only in accordance with visual impressions, the section on investigative studies would bring about a speedy and complete revision of this judgment. For here is ample evidence that many syndromes are but the reflexion on the skin of a disturbed lipid or protein metabolism perhaps, the outer sign of an inner pathology in some remote organ. Frequently diagnosis entails long and searching biochemical or histochemical studies.

In the beginning of the book the editors make the customary personal contribution. In this instance they write on the use of superficial X-rays in dermatology, an informative and timeous article, since it is doubtful whether therapeutic aid is being employed to the fullest advantage.

Out of 460 pages all that can usefully be said about the venereal diseases is comprised in 13 pages—an eloquent testimony to the efficacy of the antibiotics in this field.

C.K.O'M.

TRAINING OF SANITARY ENGINEERS

The Training of Sanitary Engineers; Schools and Programmes in Europe and in the United States. By Milivoj Petrik. Geneva, 1956 (*World Health Organization: Monograph Series*, No. 32). 151 pages. Price: £1, $4.00 or Sw. fr. 12. French edition in preparation. Local Sales Agent: Van Schaik's Bookstore (Pty.) Ltd., P.O. Box 724, Pretoria.

In almost every country the demand for qualified sanitary engineers far exceeds the ability of existing educational institutions to supply them. This lack of opportunity for specialized study in a field of great importance to health improvement is of concern to WHO; and, in an effort to increase recognition of the need for sanitary engineers and to encourage development of facilities for training them, WHO, among other relevant activities, sponsored a symposium on the training of sanitary engineers in Europe. In preparation for this symposium, Professor Milivoj Petrik, of the University of Zagreb, Yugoslavia, made an extensive survey of European schools and programmes. Professor Petrik's findings and his comments thereon form the body of this monograph.

It is believed that information of the type contained in Professor Petrik's survey has never before been assembled in one publication. By means of personal visits, correspondence, and study of the available programmes, the author collected all the

information he could concerning training in sanitary engineering in 16 European countries—Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, the Netherlands, Portugal, Spain, Switzerland, Turkey, the United Kingdom and Yugoslavia. In addition, he undertook a review of sanitary engineering education in a selected number of teaching institutions in the USA. Details concerning the curricula offered in 10 accredited schools of public health, the engineering faculties of 13 universities, and the Massachusetts Institute of Technology are given for purposes of comparison with European courses.

A report on the symposium itself appears in an annex to the text proper.

This survey reveals great disparities among European countries in the education offered in, and recognition accorded to, sanitary engineering as a special branch of engineering. It calls attention to fundamental needs and, through comparison with sanitary engineering education in the USA, offers suggestions for further developments in Europe and other parts of the world.

P.M.S.

DISEASES OF THE NOSE AND THROAT

Diseases of the Nose and Throat. A Textbook for Students and Practitioners. Sixth Edition. By Sir St. Clair Thomson, M.D., F.R.C.P. (Lond.), F.R.C.S. (Eng.), LL.D (Hon.), Winnipeg. Pp. 1040 + xvi, with illustrations and colour plates. 90s. 0d. London: Cassell and Company Ltd. 1955.

Contents: 1. Introductory. 2. Diseases of the Nose. 3. Diseases of the Accessory Sinuses (Paranasal Sinus Diseases). 4. Tumours of the Nose and Accessory Sinuses. 5. Diseases of the Naso-Pharynx. 6. Diseases of the Pharynx and Tonsils. 7. Diseases of the Larynx. 8. Diseases of the Trachea and Bornchi. 9. Diseases of the Oesophagus. 10. Foreign Bodies. Peroral Endoscopy. 11. Chronic Infective Diseases. 12. Acute Specific Fevers in the Nose and Throat. 13. The Nose and Throat in some General Affections. Formulae. Index.

The 6th and latest edition of this well-known work places the emphasis mainly in the field of treatment. The general structure of the book has changed but little since the previous edition was published in 1948. The arrangement of plates and radiographs has been slightly altered and the number of figures reduced to make space for the necessary expansion of the text.

Sir Harold Gillies has reviewed the section on the plastic repair of the nose and several new illustrations have been provided.

Stridor, although a symptom and not a disease, has been conveniently considered under a single heading. In the past there has been considerable confusion in nomenclature, and in this edition of the book the arrangement differs in certain respects from that adopted in the previous edition. A series of coloured illustrations of the larynx in childhood has been included in this chapter.

The chapter on Nasal Allergy is very much the same as in the 5th edition. Treatment of this depressing condition does not seem to have advanced much, if at all, in the last 10 years.

The treatment of tuberculosis of the upper air passages has been fully brought up to date in keeping with modern trends.

R.J.V.M.

ALGAE AND PLANKTON

The Role of Algae and Plankton in Medicine. By Morton Schwimmer, M.D. and David Schwimmer, M.D. Pp. 85. $3.75. New York: Grune & Stratton, Inc. 1955.

Contents: Foreword. I. Introduction. II. Definitions and Classifications. A. Algae, B. Plankton. III. Macroscopic Algae (Seaweed). A. Nutritional Aspects, B. Medicinal Uses, C. Miscellaneous Uses. IV. Plankton. A. Zooplankton. B. Phytoplankton (Microscopic Algae). 1. General Nature. 2. Metabolism, Culture, and Nutritional Values. 3. Medical Aspects. a. Water Supply and Sewage Disposal. b. Animal Intoxication. c. Human Intoxications. V. Discussion. Bibliography. Index.

This monograph deals mainly with the nutritional value of algae and of plankton. The use of seaweeds and of their derivatives as foods and as therapeutic agents is traced from legendary to modern times and some of the latest uses of alginates are described. Zooplankton has been investigated as a protein-rich food, and phytoplankton has been cultivated to this end; some recent experiments on the artificial culture of *Chlorella* are described, which have given promising results.

Outbreaks of algal poisoning in domestic animals are reported from many parts of the world, including South Africa. Direct algal intoxication is rare in man but some cases of poisoning following the ingestion of fish are attributed to algae in the fishes' diet. The authors also speculate on the possible role of algae in the aetiology of a number of nervous diseases, but without adducing any convincing evidence.

The book brings together information from very diverse sources and has a comprehensive bibliography. It should prove interesting both to biologists and to the physicians for whom it is primarily intended.

A.W.S.

CORRESPONDENCE : BRIEWERUBRIEK

DOCTOR-MIDWIFE-PATIENT RELATION

To the Editor: Is it possible for Federal Council to do something in regard to the unsatisfactory status of the doctor-midwife-patient relationship?

A parturient mother is often pretty touchy, and in no state to stand the extremely tactless way she is treated in some maternity homes. Every qualified and probationer nurse who handles her gives her conflicting and tension-raising advice. Worse: her confidence in her own doctor is both subtly and blatantly undermined. Here are some examples:

1. The doctor has instructed the patient in breast emptying as popularized by Harold Waller. A nurse tells her: If you use that method, you'll develop cancer in later life.

2. Because of domestic difficulties a patient has undergone an extremely trying pregnancy. She is highly strung, and labour is premature. The child does well, but the mother's milk goes off. 'Never mind', soothes the doctor, 'we can use this Carnation milk'. Sister replies: 'Matron who has just come from overseas says this baby is too big for Carnation; after 3 weeks we put them on Cow and Gate'.

3. 'You'll never feed your baby', is a frequent reminder to the patient by the nurse. And so it goes on endlessly.

And Heaven help the obstetrician or family doctor who tries to introduce anything 'new', such as relaxation, demand feeding, rooming in—or the opposites if his technique or the patient's condition require it.

It seems to me that midwives need 3 items added to their education:

1. Simple psychology, relating especially to maternal emotional states.

2. Ordinary medical ethics—in regard to (*a*) patients' needs and (*b*) midwife-doctor relationship—and general morality, particularly in regard to libel and scandal.

3. Infant feeding: (*a*) That there is one lactogogue and one only—suckling (so neutralizing the many distractions the mother gets from advisers in regard to this injection or that food or preparation—all useless); and (*b*) that cow's milk is cow's milk and cannot be 'humanized'—the essential sameness of all cow's milk, whether it is fresh out of the udder, dried, or condensed. It is shocking how midwives follow popular opinion about this, that or the other brand of milk. Let the doctor beware who prescribes a brand other than the one the midwife acknowledges. Nor will she hesitate to tell mother, 'That milk made your baby sick—you'll have to change it'. I am quite willing to learn from midwives. I acknowledge my indebtedness to the best of them (who incidentally will agree with all I write here), but I prefer them to tell *me* what's what—not go below my belt to my patient. The undermining by the ignorant or tactless type of midwife of the doctor-patient relationship in many cases exceeds the limits of ordinary human decency, and many of our better-class midwives are finding the situation just as exasperating as the doctors. So far as I know, the doctors try to give their patients confidence in the maternity homes and staff. Are we not entitled to a *quid pro quo*?—and that entirely for the sake of the patient, for it is in the public interest that there should be not only doctor-patient rapport, and doctor-nurse rapport, but doctor-patient-nurse rapport.

Quot homines tot sententiae

15 October 1956